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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Marnix L Bosch

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EXAMINER

DRODGE, JOSEPH W

ART UNIT

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1797

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/517,871	Applicant(s) BOSCH ET AL.	
	Examiner Joseph W. Drodge	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40 and 60-69 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 of copending

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Application No. 10/992,154. Although the conflicting claims are not identical, they are not patentably distinct from each other because they commonly comprise methods of using cross-flow membrane filtration to enrich recirculating solutions in leukocytes so as to culture stem cell populations.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, “the sample...” lacks antecedent basis or is inconsistent with “cell population”.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5,12,13,23,25 and 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Brody et al patent 5,922,210. Brody et al disclose a tangential flow filtration device comprising remover unit having cross-flow chamber 4/6, filtrate chamber 3, filter 5, inlet 1 to direct flow parallel to the filter, centrally disposed outlet 7 opposite/facing the filter surface, the filter having a possible range of pore sizes overlapping 1-10 microns (column 3, lines 50-57, column 5, lines 18-23 and column 6, lines 20-24), such that the flow across the filter enriches a sample population of blood containing either red blood cells, white blood cells (leukocytes), or both (column 4, lines 1-8) .

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Brody discloses the following for dependent claims: for claim 2, “means for providing predetermined input rate and filtration rate (column 6, lines 31-44), the filtration rate optionally the input rate; for claims 3-4, pore size of about 3-5 microns, for claim 5, blood source . i

For independent claims 23-25, Brody also discloses , the device being used in sampling and analysis (column 1, lines 20-35) the inlet being disposed above the filter (column 3, lines 18-19, or column 6, lines 38-40 “applying of gravitational forces”) and outlet 7 being optionally disposed to upper portion of cross-flow chamber 3; use of gravitational forces implies flow of feed liquid being above or across the top of the membrane filter. The flow rate may be increased or decreased through the filter (column 6, lines 31-49 concerns starting and stopping of pressure applying to start and stop flow and also backflow through the filter at times at about half the rate of pressure and flow during filtration mode). The filter 5 appears to be horizontal with the top plane of chamber 6.

Column 4, lines 1-8 of Brody discloses blood, plasma, and red and white blood cells ("erythrocytes" and "leukocytes") for claims 27-29, hence inherently platelets are also present; any population of leukocytes necessarily contains some amount of monocytes.

Regarding claims 12 and 13, Brody discloses handling/separation/processing of the fluids both upstream (column 4, lines 29-31) and downstream for further processing of the fluids (column 4, lines 43-46).

For claim 33, disclosed “electroendoosmotic forces” together with “surface tension forces” (column 6, lines 39-41) overlap recited applying of tangential forces.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brody et al patent 5,922,210.

Claim 24 differs in explicitly requiring predetermined concentration of blood cells to about 10 (7th-10th power)/milliliter, filtration rates of 1/5 to 1/100th the predetermined input rate. Recitation of column 6, lines 32-40 of applying multiple positive and negative pressure to the flow obviously encompasses any range of increasing or decreasing filtration rates.

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Concentrations of blood cells is obviously a factor of both selection of blood source(s) and membrane filter pore sizes utilized.

Claims 31 and 32 differ in explicitly requiring an enriched cell population of at least about 20% or at least about 60% leukocytes. Similarly, proportion of leukocytes in cell population would obviously vary with selection of blood sources and membrane filter pore sizes.

Claims 6-10,26,30,40-48 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brody et al patent 5,922,210 in view of Castino, of record.

Castino et al teach a method and system for separating leukocytes from blood sources originally obtained as whole blood samples from human patients or donors. The blood is introduced into cross-flow membrane-containing remover units 11 and 21 through respective inlets where leukocytes are selectively removed from other blood components and constituents to form cell populations that are enriched for leukocytes. The respective retentate populations are continuously recirculated between cross flow membrane 24 in chamber 21 and cell recovery unit ("CPAS reservoir", column 4, line 63-column 5, line 10, column 6, lines 21-29, etc.) to cell populations enriched in forms of leukocytes ("production broth" and CPAS reservoir), respectively. Castino also teaches the following: the cell populations being prepared by samples upstream filtration or leukophoresis, the blood constituents naturally contain plasma, platelets, erythrocytes, etc. and the recycling of stream volumes may be carried out indefinitely (column 14, lines 45-50),[as required in claims including claims 42-47]. Castino further discloses means for heating to controlled temperature and control of filtration flow rates, filter pore size of about 3-5 microns or adapted to retain leukocytes [claims 41,46,47], blood sources, recovery

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unit and crossflow filters being in loop format and connected by inlets and outlets to the units (figures, [for claims 7-10,49 and 50], means for culturing [claims 14].

Claims 6,26 and 42 and claims dependent therefrom differ in requiring a leukophoresis device to be the blood source, although Brody et al disclose previous handling and separation of the blood source (column 4, lines 30-32). It would have been obvious to one of ordinary skill in the art to have employed the leukophoresis device of Castino in the Brody system in order to control and tailor the amount of leukocytes in the permeate or retained/enriched fluid fractions.

Claims 7-10 and 40-48 differ in requiring recirculating of blood sample fluid through the unit as outlined in claims 7-10 as involving a recovery unit with communicating with cross-flow chamber in loop/recycling format, by communication of the inlets and outlets of the chamber and unit. It would have been obvious to have employed the recovery unit and recycling loop of Castino in the Brody device or method, to result in achieving much greater purity of blood components and constituents in fluid fractions.

Claim 30 requires repeating of steps plural times to form enriched populations of leukocytes. Castino infers the recirculating process being continuous or constant, hence cell populations pass across the cross-flow membrane any number of times (column 5, lines 5-10).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brody et al in view of Castino, as applied to claims 1-10 above, and further in view of Raehse et al patent 4,751,003 or Harm et al patent 4,722,902. Claim 11 additionally requires the crossflow chamber to be cylindrical. Both Raehse and Harm (figures, etc. show such cylindrical filter membranes for crossflow separation of blood components. It would have been also obvious to have utilized

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cylindrical filter membranes of Raehse or Harm also to enhance separation efficiency, since crossflow in such blood separations has been shown to result in near 100% separation rates (Abstract of Raehse).

Claims 14-22, 34-39, 49-59 and 61-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brody et al in view of Castino, and further in view of Kopf patent 6,214,221 and/or Yamanishi et al publication US2003/0134416 (patent 6,949,355), based on provisional applications 60/394,517; 60/348,228 and 60/328,724, filed on 7/9/2002; 10/29/2001 and 10/11/2001, respectively.

These claims differ in additionally requiring various means and method steps to enhance culturing of and growth of the concentrated leukocytes or substances being derived therefrom, including beads, cell-adhering substrate and screen, tissue culture vessel to receive mature cell cultures, separate mature from immature cell cultures, temperature control means, and wash and drain lines. Castino teaches constant recirculation of fluid between crossflow membrane and recovery unit (column 5, lines 1-19 and column 6, lines 3-13).

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48, 71, 94, 96, 131-139 and 148 of the PG PUBS Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49).

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48, 71, 94, 96, 131-139 and 148 of the PG PUBS

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Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49).

Kopf teaches usuch cell culture media substrates and cell culturing and maturing method steps and system components (column 7, lines 50-67), washing and draining means (column 10, lines 47-50), antigen/antibody binding substances and substrates (column 9, lines 35-53), culture growth, nurturing \ and derivation of populations of cells (column 14, lines 35-40), separation of mature from immature cells (column 11, lines 20-49). The patent teaches use of beads (column 12, lines 25-35), separation of mature from immature cells (column 11, lines 20-49), and temperature control (column 13, lines 37-47).

It would have also been obvious to have augmented the crossflow filtration loop and recycling system and method of Brody et al in view of Castino, with the various means to culture leukocyte-derived substances and cells and stem cells, as suggested by Yaminishi or Kopf, so as to both enrich leukocyte-product cell populations and promote growth and maturing of cell cultures, so as to have a complete cell growth and culturing system in one convenient and central location, to avoid loss of cell populations and leukocyte ingredients that would otherwise result were transport of cell cultures between processing facilities.

Claims 61-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brody et al in view of Castino as applied to claims 1-10,12,14,33,40-48 and 60 above, and further in view of Yamanishi et al patent US2003/0134416 (patent 6,949,355), based on provisional applications

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60/394,517; 60/348,228 and 60/328,724, filed on 7/9/2002; 10/29/2001 and 10/11/2001, respectively.

These claims differ in additionally requiring various means and method steps to enhance culturing of and growth of the concentrated leukocytes or substances being derived therefrom, including beads, cell-adhering substrate and screen, tissue culture vessel to receive mature cell cultures, separate mature from immature cell cultures, temperature control means, and wash and drain lines.

Yamanishi teaches such cell culture media substrates and cell culturing and maturing method steps and system components (paragraphs 48,71,94,96,131-139 and 148 of the PGPUBS Publication). The patent teaches use of beads (column 7, lines 50-67), washing and draining means (column 5, lines 53-column 6, line 12), antigen/antibody binding substances and substrates (column 8, lines 5-38), culture of stem cells (column 9, lines 57-67), separation of mature from immature cells (column 11, lines 20-49). It would have also been obvious to have augmented the crossflow filtration loop and recycling system and method of Brody et al in view of Castino, with the various means to culture leukocyte-derived substances and cells and stem cells and recirculate and return cell populations, as suggested by Castino and further suggested by Yaminishi, so as to both enrich leukocyte-product cell populations and promote growth and maturing of cell cultures, so as to have a complete cell growth and culturing system in one convenient and central location, to avoid loss of cell populations and leukocyte ingredients that would otherwise result were transport of cell cultures between processing facilities.

Applicant's extensive arguments with respect to claims 1-69 have been considered but are largely moot in view of the new ground(s) of rejection. Brody much more clearly disclose

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tangential fluid flow through a cross-flow filtration membrane with a centrally disposed flow outlet, the filtration membrane having a pore size range overlapping all of the instantly recited pore size ranges and optional selective removal or retaining of blood or plasma sample/analytical cell populations depleted or enriched in leukocytes and erthrocytes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Drodge at telephone number 571-272-1140. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Roy Sample, can reached at 571-272-1376. The fax phone number for the examining group where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either private PAIR or Public PAIR, and through Private PAIR only for unpublished applications. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JWD

April 16, 2008

/Joseph W. Drodge/
Primary Examiner, Art Unit 1797